

From the
Institute for Pathological Anatomy of the University of Basel (Switzerland)
(Director: Prof. A. A. Werthemann)
Work under the supervision of Prof. F. C. Roulet

Reticulum Cell Sarcoma in Childhood with a Presentation of a Case

INAUGURALDISSERTATION

zur Erlangung der Doktorwürde der Medizinischen Fakultät
der Universität Basel

by

STANLEY CZEPIEL

Paterson, N. J., U.S.A.

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Buchdruckerei E. Birkhäuser & Cie. AG.

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Von der Medizinischen Fakultät genehmigt auf Antrag von
Prof. *F. C. Roulet*.

Tag der Promotion: 22. November 1952.



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Reticulum Cell Sarcoma in Childhood with a Presentation of a Case

Presenting a case of Reticulum cell sarcoma in an infant 8 months old. The condition being only then suspected when a week before death a enlarged lymph node in the inguinal region was observed and a biopsy taken (puncture). Child at this stage was in such a moribund state that nothing further diagnostically could be done.

In my consideration of this case it is not my purpose to review Reticulum cell sarcoma for all the age groups but to try to limit myself to the childhood or pediatric group (0-13). Tumors in childhood are a relative rarity but VIDEBAEK³⁹⁾, in his treatise *Malignant tumors in childhood*, shows that the incidence of malignant disease is about 1-2 cases per 10,000 children. About 4% of all deaths among children is found to be due to malignant tumors, of which the most common in this period are the sarcomas and mixed tumors. At the Institute for Pathology of Basel from the year 1934-1951 there have been 48 autopsied cases of Reticulum cell sarcoma and of these only 2 were in the so called age group: the case I am presenting and a 14 year old female. A limited number of cases are found in the literature over this particular age period: AHLSTROEM³⁾ a 11 year old female, ROULET²⁸⁾ a 11 year old male, LANG and ZIERHUT²⁰⁾ a 7 year old female, BENECKE⁷⁾ a 4½ year old male, AHLSTROEM⁵⁾ a 3 year old female, KNOPF¹⁹⁾ a 2½ year old female, NOBICOURT and LIEGE²³⁾ a 18 month old female, CZERMAK and ROSENKRANZ¹¹⁾ a 3 month old female, DAWSON, INNES, and HARVEY¹²⁾ had 9 cases in children up to 5 years of age. Then there were 3 cases which were proven by biopsy and operative removal, these are GROSSO¹⁷⁾ a 9 year old female, COMELLI⁹⁾ a 10 month old female, AHLSTROEM²⁾ a 7 month old female.

Case presentation)*

A 6 month old female child who has been sick for about 10 days. Fever at one time was 40°C. Did not want to drink. Had a bit of a cold and rhinitis also the mother thought that the child had pain on coughing. Urine had a penetrating odor. Diapers were colored dark yellow. In January the other children in the family had had the grippe. Family lives in rather crowded quarters. Doctor that was called, diagnosed a pyuria and treated with sulfa drugs. Cough became more marked and mother quite upset so child sent to the hospital. Admitted on February 24, 1940. Diagnosis from private doctor was influenza, tracheitis, and pyelocystitis.

*) My sincere thanks to Prof. FREUDENBERG for his permission to use and present the case history and hospital progress of the case I am presenting.

Physical examination on admission

Delicate child, pale and tired in appearance.

- Skin: Normal fat distribution with slight loss of skin turgor.
- Head: Freely moveable. Border of the large fontanelle is soft. Small fontanelle is closed. Craniotabes palpated.
- Eyes: Slight conjunctivitis.
- Nose: No discharge.
- Ears: Ear drums on both sides are covered with a waxy material.
- Mouth: Mucosa is normal. Tongue is furred. No teeth are present. Tonsils are not enlarged. Pharynx is reddened.
- Neck: No thyroid enlargement. Lymph nodes at angle of mandible are pea sized, cervical group slightly smaller.
- Thorax: Well formed, symmetrical. Costochondral junctions are enlarged. Heart normal. Lungssibilant and dry rales.
- Abdomen: Liver and spleen are not enlarged. Umbilicus normal.
- Genital: Normal.
- Extremities: Slight swelling felt at the epiphysis.
- Neurological: Not found in history.

Tentative diagnosis was made of rickets with latent tetany, rhinitis, otitis media, pharyngitis, and conjunctivitis. Massive dose of vitamin D given for the rachitis and CaPo_4 for 14 days.

Hospital progress

- February 27: Examination of the lungs revealed that sibilant rales were less perceptible but that there were still large numbers of rales heard at the bases. Fever 38°C . and remained so for 14 days. Pharyngitis did not respond to steam therapy. R.B.C. count 4,380,000. Hbl. 75. Color index 0.87.
- March 14: *B. coli* found in the urine and then 4 days later a severe conjunctivitis noticed with bilateral involvement. Otitis media both ears. Pirquet reaction negative.
- March 27: Temperature 39°C . Pus from nose, mouth, eyes and ears. R.B.C. count 3,950,000. Hbl. 53. Color index 0.98. Transfusion of 150 cm^3 of blood. Sulfa started next day for 4 days.
- March 28: R.B.C. count normal. Hbl. 74. Color index 1.0.
- March 31: Temperature again afebrile, child more lively. Secretions still present.
- April 4: Child appears to feel better. Secretions have decreased.
- April 8: Temperature 39°C . with an increase in the secretions. Sulfa tried again but with no success.
- April 14: Moro reaction negative.
- April 15: 6 days before death in the left inguinal region an indolent, somewhat blue colored lymph node observed. Movement of the left leg causes pain. Nothing seen on the right side. Liver and spleen palpable. No other lymph node swellings are noted. R.B.C. count 2,670,000. Hbl. 59. Color index 1.13.
- April 16: Blood transfusion 150 cm^3 .
- April 18: Lymph node puncture done. Report was numerous giant cells with many nuclei. Reticulo-endothelial involvement now considered.
- April 19: Tibia puncture made for bone marrow bacteriological study.
- April 20: Secretion from eyes, ears, nose is profuse. Mouth has a strong Foetor ex Ore. Border between hard and soft palate is ulcerated as is the inside of the lower lip. Exitus after 2 months in the hospital.

Laboratory and diagnostic procedures

Blood chemistry	Ca 8.9%	Po 1.17%	(no phosphatase done)	
Blood reports	March 18	March 27	April 15	April 19
Hbl.	—	53%	59%	76%
R.B.C.	—	3,950,000	2,670,000	3,310,000
C.I.	—	—	1.13	1.15
W.B.C.	5,250	4,700	5,300	3,550
Myeloblasts	—	—	—	—
Myelocytes mature	—	—	—	—
Myelocytes immature	—	—	1%	2%
Polymorphs	19	30	33	21
Eosinophiles	0	0	0	0
Basophiles	0	0	0	0
Monocytes	5	7	3	3
Lymphocytes	69	34	47	57
Plasma cells	0	0	0	0
Juvenile forms	11	29	16	17
	Anisocytosis	Same as	Same as	Same as
	Polychromia	preceeding	preceeding	preceeding
	Leucocytes	report	report	report plus
	toxic granules			more toxic
				granules

Urine analysis

	March 14	March 18	March 26
Albumin	Small trace	Small trace	Small trace
Sugar	—	—	—
Casts	—	—	Granular
Pus cells	Few	Few	Rare
Bacteria	Many	None	None

Bacteriology

March 27: Throat.—No diphtheria, streptococcus or staphylococcus.
 April 9: Pus.—*Staphylococcus aureus halmolyticus*.
 April 17: Pus.—*Staphylococcus aureus halmolyticus* and diphtheria.
 April 25: Bone marrow.—*Bacterium pyocyaneus*.

Lung X-Ray

Shadow on the right side, appears to be a pneumonic infiltration. An enlargement of the hilar lymph nodes also noted. X-ray of the pelvis shows no pathological changes.

Clinical discussion

Case clinically as a Reticulo-endothelial process wether benign or malignant was practically impossible to diagnose from the presenting symptoms. That advanced rickets was present can be seen from the following symptoms:

1. Enlargement of the costochondral junctions.
2. Slight swellings at the epiphysis of the extremities.
3. Soft border of the large fontanelle.
4. Craniotabes.
5. Blood chemistry.—Ca 8.9%, Po 1.17% (no phosphatase done).

This condition was a probable predisposing factor for the respiratory infection which then spread so rapidly. MITCHELL²²⁾ states that rachitic children are particularly prone to infection of the mucous membranes of the respiratory airways. No marked anemia on admission. Blood picture was normal but within a

month it had sunk from 4,380,000 to 2,770,000. This anemia might probably have been due to the prolonged infection and toxic state of the child. Transfusion of 150 cm³ of blood and next day the count was up to 3,950,000 with a Hbl. of 74%. On the 15th of April blood count was again down to 2,670,000 with a Hbl. of 59%. Another transfusion of 150 cm³ given. Was this destruction of the red cells due to a hemolytic process or to a malfunction of the hematopoietic system? Bone marrow studies were not done, so we cannot answer that question. Leucocyte studies showed, in the four counts done, a low white count which with the massive infection which was present brought up a diagnostic problem as to whether it was a aleukemic leukemia. Normal count for this age group should be 9,000–9,200 cells, however the differential definitely shows a shift to the left but no abnormal forms seen. Bacteriological studies of the pus revealed a *Staphylococcus aureus halmolyticus* and studies of the bone marrow showed a *B. pyocyaneus* infection. Bacteriology department suggested the possibility that it might be skin contaminant, and as no repeat reports were possible due to the child's death, why the marrow infection is doubtful. First clinical evidence came 6 days before death with the sudden appearance of the swollen lymph gland in the left inguinal region, with a palpable liver and spleen. Of significance here is the fact that of the normally palpable nodes of the body only this one was enlarged. As a diagnostic procedure a puncture biopsy was done which revealed that there were numerous giant cells with many nuclei. All we can surmise from this is that a Reticulo-endothelial reaction was going on, perhaps of an infectious nature or possibly of a malignant form. No further studies done such as bone marrow analysis or an extirpation of a gland for histological study. Another possible lead was the X-ray of the lungs which showed a pneumonic infiltration and a hilar enlargement. This latter could very well have been purely from the pneumonia, bronchitis, and the tracheitis. Pelvic films revealed no pathological processes. Before any other diagnostic procedures could be done the child died.

Clinical diagnosis at time of death was:

1. Rickets.
2. Questionable Reticulo-endothelial system involvement.
3. Aleukemic leukemia.

Clinical differential diagnosis:

1. Infectious mononucleosis.—Clinical picture is a lymphocytosis with a predominance of monocytic elements or better known as Downey cells. Cervical lymph nodes usually involved and spleen enlarged in about 50% of cases. In this case only slight monoresponse and no lymphocytosis, instead a leucopenia.
2. Agranulocytosis.—Here we get a neutropenia and a leucopenia, typical sore throat, ulcerations of the mouth, swollen cervical lymph nodes. Drug use over a certain period usually associated. This case had a leucopenia but no neutropenia and no history of receiving agranulocytic drugs except Sulfa which was only given a few days. Main difference however is that our white count was only 3,550 which is not low enough for an agranulocytosis where count is around 500–1,000 cells. CECIL⁸) states that when counts get around 2,500 then agranulocytosis must be doubted.
3. Aleukemic leukemia.—A possibility but due to our not finding any pathological forms in our leucocyte studies we can practically rule this condition out.
4. Lymphogranulomatosis.—Relatively rare in infants. Symptoms of lymph node swelling, usually cervical with a Pel-Epstein type of fever curve, plus leucopenia. This case first a very young infant, solitary inguinal lymph node swollen and continuous fever curve speaks against it being a Hodgkins.

5. Brucellosis. -Also affects the lymph nodes and spleen. Symptoms are cough, malaise, anorexia, joint pain and fever of an undulating type. Children are less frequently affected than adults. This not very probable here as we have a definite infection to account for our continuous fever curve. No serological studies were done.
6. Tuberculosis ruled out by the negative tuberculin reactions which were done a month apart.
7. Syphilis. Symptoms are coryza, skin eruptions, pseudoparalysis and moist lesions around mouth, anus and genitalia. Spleen and liver are enlarged. In the discussed case this condition improbable because child was well up to the 6th month, no pseudoparalysis and no moist lesions around mouth, anus and genitalia.
8. Histoplasmosis. -Disease picture with fever, anemia, leucopenia and enlargement of the liver, spleen and lymph nodes. Ulcerative skin lesions and occurs more frequently in adults. Discussed case had no generalized node swelling, no skin ulcerations and no loss of weight.
9. Toxoplasmosis. -Rare and usually encephalitis and convulsions. No such indication in this case.
10. Malignant tumor metastasis. -Possible but in this case with only the puncture biopsy to go on would be difficult to say whether metastasis or primary.
11. Other diseases that should be considered are leishmaniasis, malaria, bartonellosis, trypanosomiasis, relapsing fever and glanders are mentioned but not discussed because of geographical situation and no contact history.

AUTOPSY REPORT: NO. 452/40.

Description of the body

Body of a rather cachectic female child without rigor mortis, still somewhat warm. Skin is flaccid, yellowish and somewhat moist. Only a few livores are present on the dependant parts and they are easily pressed away. On the upper and lower lips mostly on the inside are fine ulcerations and rhagades. In the region of the right tibia are signs of a medical procedure. In the left cubital fossa is a small operative incision.

Description of the organs in situ

Subcutaneous tissue is moist and contains abundant fluid. Musculature is pale red. On opening the abdomen the large spleen and liver are apparent. Both extend beyond the thoracic cage border by more than 2 fingers. The omentum, which has little fat but which is very rich in fluid, covers the intestine. Urinary bladder is moderately filled. Diaphragm rises on the right to the 4th intercostal space and on the left to the 5th intercostal space. The costochondral junctions show beadlike swellings. With the opening of the thoracic cage it is noted that both enormously bloated lungs touch each other, they seem very pale at the edges. Thymus is small, it lies on the fatless pericardium. On cutting it is moist, pale and yellowish.

Description of the thoracic contents

The pericardium contains very little clear fluid. Heart is very flaccid with a dilatation of the right side. Pulmonary and aortic valves are soft, tricuspid because of the dilatation on the right side is not completely sufficient. Mitral valve is soft. Foramen ovale is open. Myocardium shows cloudy swelling and is very pale and edematous.

The left lung is pale, large, and everywhere in the lung tissue but especially in the apical and the paravertebral areas are tough, gray reddish inclusions. The cut surface of the upper lobe is pale in the dependant part and somewhat reddish yellow. In the apices the pulmonary tissue is reddish gray and contains no air. In the lower lobes are isolated areas which are granular, containing no air and dark colored. These areas are sharply demarkated from the surrounding somewhat lighter yellowish pulmonary tissue. The right lung is also greatly bloated and large. In the apical region of the upper lobe and then again in the lower lobe are reddish gray tough foci containing no air and some of these foci are sunk below the surface of the lung. Occasionally it is possible to find fine whiteish strands of small barely visible nodes in the lung tissue. The hilus glands are medium large, reddish gray and soft. The bifurcation glands are reddish gray and partially pitted. Pulmonary vessels are soft. Bronchi are reddened and contain yellowish masses in the narrowest branches.

Cervical organs

Tongue is clean and base of the tongue is rather small. Tonsils are small. Thyroid is small, light reddish gray and somewhat dulled on cut surface. Larynx is soft. Trachea pale. Esophagus clean it's entire length. Paratracheal lymph nodes are reddish gray and moist.

Abdominal organs

Spleen is large, dark reddish gray on the surface (cut) and rather firm. Trabeculae recognizable. Follicles and blood vessels are not sharply defined. Liver is large and has a yellowish brown color. Whereas in the peripheral regions the tissue is partially sprinkled with a more intense yellow. Parenchyma shows cloudy swelling and appears moist. Gall bladder contains a watery, bright yellow mass. The larger bile passages are patent. The mucous membrane is soft. The left adrenal is moist. The pattern is unclear and the cortex is only slightly yellow. Right adrenal is somewhat smaller. Here also the cortex is only slightly yellow and the medulla is very pale. The left kidney seems enlarged and the capsule is easily separated. Fetal lobulation is preserved. Parenchyma is pale and rich in fluid. Medullary border is sharply defined. Cortex is wide. The mucous membrane of the pelvis and ureter is delicate. Right kidney has a wedge shaped indentation in one place. At this indentation small cysts were seen. Urinary bladder is rather wide, vagina is narrow, uterus is elongated. Mucous membrane of the uterus is rather pale. Ovaries are pale and small. Para-aortic lymph nodes are soft and pitted, enlarged and very vascular. Some of them grow around the whole aorta. The iliac and femoral arteries especially on the left side are completely surrounded by large, pitted and often very vascular, swollen lymph nodes. Here and there it is possible to find yellowish inclusions in the nodes. The marrow of the ribs and vertebra is reddish gray and rich in fluid.

Gastro-intestinal tract

In the appendix there is very little mucus. The large intestine is distended and contains a somewhat slimy yellowish mucus which is slightly adherent to the mucosa. The small intestine also contains a lot of this yellowish mucus. Mucosa of the intestine is rather pale and the lymphatic apparatus is scarcely visible to the naked eye. The lymph nodes of the mesentery are small. The mesentery contains little fat. Pancreas is narrow and of lobular construction with a soft consistency.

Brain

Skull opened according to the tentorium method. Quite a bit of cerebral spinal fluid flows out. Brain is firm and the gyri are narrow. Meninges contain very little

blood. On the cut surface the brain contains much fluid. Pattern is symmetrical. Nuclei of the basal ganglion and the cortex are not yet clearly demarcated. Lateral ventricles and 4th ventricle are wide. The cerebellum is rather soft compared to the cerebrum. Pons and medula oblongata are rather firm.

Weights of organs

		Normal weights for this age (MITCHELL) ²²
Length	67 cm	70.3 cm
Body weight.	? g	—
Heart.	39 g	50 g
Left lung	47 g	55 g
Right lung	66 g	55 g
Spleen	70 g	30 g
Kidneys	85 g	65 g
Liver	340 g	300 g
Brain	? g	900 g
Thyroid	2 g	3 g
Thymus.	3 g	20 g
Adrenals	7 g	6 g
Head	42 cm	
Thorax	40 cm	

Pathological anatomical diagnosis

Confluent hemorrhagic bronchopneumonia of both lungs with advanced emphysema. Reticulo-endothelial sarcoma of the paraaortic, iliac and inguinal lymph glands on the left side with signs of hemorrhage of the entire lymphatic tissue. Slight swelling and sarcomatosis of the bifurcation and paratracheal lymph glands. Advanced hyperplasia of the spleen and liver parenchyma. Edema of the renal tissue. Slight hydrocephalus internus and externus. Fresh hemorrhages in the abdominal cavity with signs of attempted splenic puncture. Advanced involution of the thymus. Slight meteorismus. Hemorrhagic diathesis. Fine septic ulceration of the skin of the lips. General anemia and cachexia.

Histological description of the organs

Bone marrow: Vertebra.

All the stages of erythropoiesis and myelopoiesis are present and the marrow is exceptionally dense and rich in cells. The development of the blood elements seems to be proceeding normally. Aside from the normal elements of the bone marrow there are many cells with weakly staining cytoplasm without granules with occasional vacuoles and with sharply defined nuclei. The nuclear membrane in these cells is especially prominent. The chromatin is finely distributed and the nuclei appear round, oval, occasionally indented and kidney shaped. The cell forms are not round but slightly branched. Here and there they form clusters and nodes which are not sharply demarcated. Occasional mitotic activity is seen in these cells. The marrow giant cells are not all of the same type, probably the greater majority are composed of uncharacteristic megacaryocytes. There are however other forms in which two or more nuclei oval to bizarre in shape occur and in which the chromatin framework appears to be much looser than that of the megacaryocytes. Their cytoplasm also lacks granules. Gomori stain shows a clearly defined reticulum framework. Occasionally it seems to be slightly thickened

especially in those regions where the somewhat primitive appearing cells (reticulum cells) occur in clusters, otherwise it is generally unchanged.

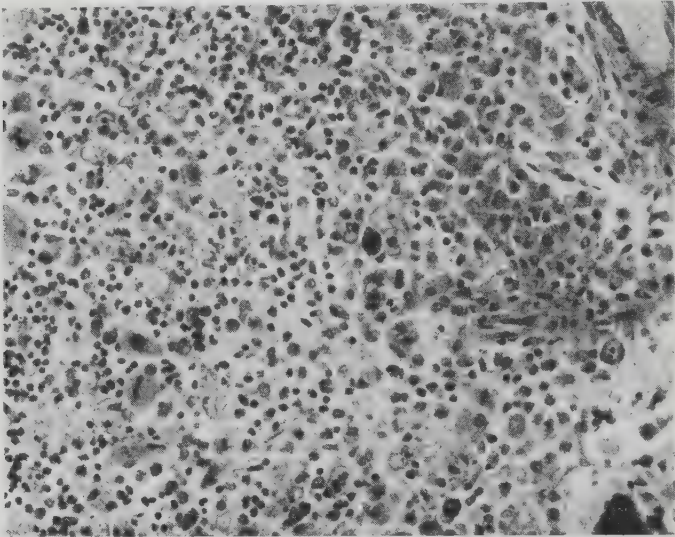


Fig. 1.--Bone marrow 210. Normal blood elements plus cells which lie in loose groups. A focal hyperplasia of reticular cell elements pointed out by arrow.

Lymph gland

Is not to be recognized as such because of the complete destruction of the normal lymphatic tissue and follicles. Some small islands of lymphocytes may be

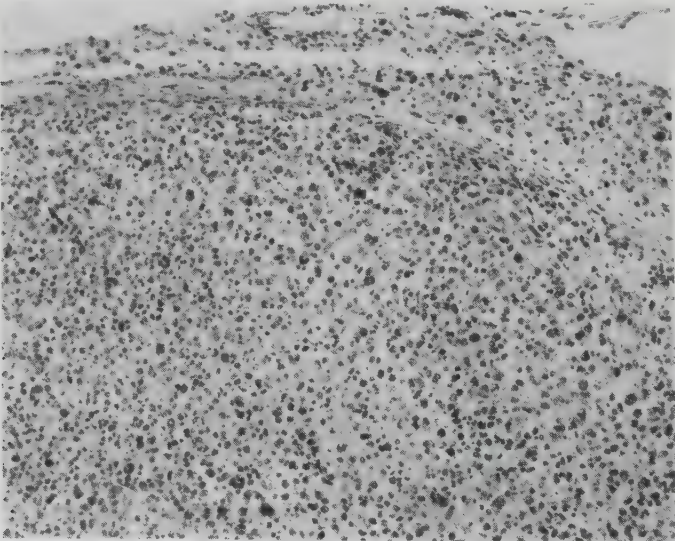


Fig. 2.--Lymph node 100. HE stain. Lymphatic structure is destroyed. Polymorphous admixture of cells. Invasion and breakthrough of the capsule with cellular elements seen.

seen. Through the whole gland there is a polymorphous admixture of cells of which the most striking are the numerous giant cells which have two or more nuclei.

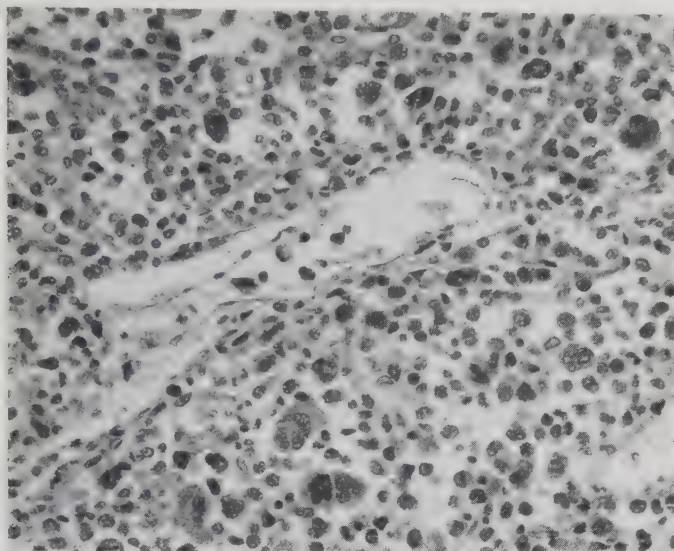


Fig. 3. Lymph node 210. HE stain. Giant cells with 2 or more nuclei oval to bizarre in shape. Cells are found singly and in clusters. Appear to have cytoplasmic prolongations.

The giant cells are oval to bizarre in shape. They appear to have prolongations or cytoplasmic expansions and seem to interweave between the cells. Protoplasm is pink stained and the nuclei are oval to kidney shaped, showing basophilic granular

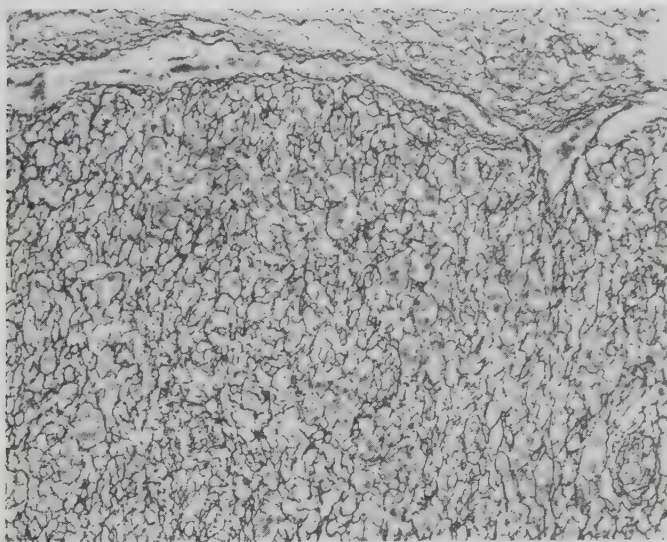


Fig. 4.—Lymph node 100. Gomari stain. Shows a increase in the reticulum, with a diffuse increase in the fibrillary elements.

stippling of the chromatin. Many mitotic figures seen in the giant cells. Other elements present are epithelioid, round and plasma cells. All elements appear rich in nucleoli. All this speaks for unripe cellular elements. Peripheral sinuses completely obliterated, other sinuses are filled with the above mentioned elements. Capsule is invaded and exactly the same elements found in the fat tissue showing a break through of the process. Gomori stain shows an increase in the reticulum, clumping of the cells and a diffuse increase of the fibrillary elements and of each cell. Very small areas are delineated by these branches.

Spleen

Structure of the spleen is markedly changed. One can hardly recognize that it is the spleen. Spleen is very hyperemic almost like a sponge that has filled itself with blood. In certain areas one can still see remnants of splenic pulp and follicles. The lymphatic tissue is practically nil. Sinuses are well delineated. Pulp completely filled with blood more so than the sinuses. Reticulum cells seen in the sinuses phagocytising the red blood cells. The spleen is filled with cell elements which can be found throughout the whole gland. Prominent again are the giant cells which are numerous and are oval to bizarre shaped in form. They have from one to three nuclei and the nuclei are oval or kidney shaped with a basophilic

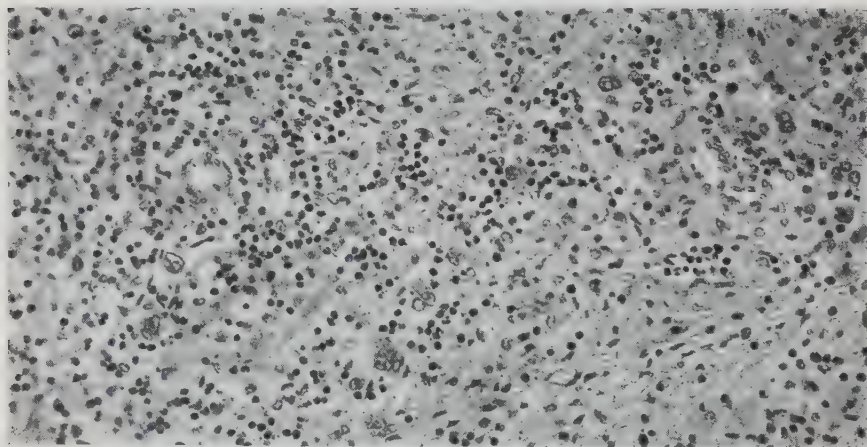


Fig. 5.—Spleen 210. HE stain. Splenic structure is not to be recognized as such. Remnants of 2 splenic follicles and within the follicle boundary giant cells are seen which appear to be enmeshed there. Spleen is hyperemic and phagocytosis is seen.

granular chromatin. These cells lie singly or in clusters and seem to be located in the remnants of the lymph follicles. As a matter of fact these cells or clusters which are so clearly seen in these follicles seem to be the cause for the replacement of the lymph follicles and pulp throughout the whole gland. No mitosis seen. Gomori stain shows a marked reticular reaction and a diffuse fibrillary formation with a coalescence of fibers.

Liver

Shows signs of passive congestion and some cloudy swelling. Cellular structure is indistinct and granular. In the liver sinuses we see that the Kupffer cells seem to be enlarged and actively phagocytising.

Large intestine

Shows that the mucosa is overlaid with mucus. The lymphatic tissue is only slightly developed and rarely one sees a large pinkly staining cell with a faintly stained nucleus. Submucosa is narrow and poor in cellular elements.

Kidney

Cell structure is indistinct and shows signs of cloudy swelling. Epithelium appears to be normal and no cellular infiltrates are seen.

Lungs

Show a marked emphysema, with a large number of coalescing alveoli. Bronchi are filled with cellular elements, inflammatory in type. Bronchioles are also filled with these elements and around the bronchioles we have a cellular cuffing. Interstitial tissue of the lung is also infiltrated.

Ovary

Germinal epithelium is well formed with large numbers of primary follicles. Rete ovarii, nerves and epoophoron are well developed. Tubular epithelium is intact. No cellular infiltrate noted.

Thyroid

Follicles are medium in size, filled sparingly with eosinophilic staining colloid. Epithelium is low or cuboidal in type.

Hypophysis

Has a rather sparse cellular structure and in the middle lobe we can see a cyst. Differentiation between cellular structure types normally found is difficult.

Pathological anatomical summary

In the presented case a definite proliferative process is invading the lymph nodes, particularly the paraaortic, iliac and inguinal chains, on the left side of the lower abdomen, with involvement of the paratracheal and bifurcation groups. To be noted at this time was that not other group of lymph nodes were involved. The lymph nodes were found to be swollen, hemorrhagic and edematous and microscopically with a complete destruction of the normal lymphatic structure with a proliferative polymorphous cell replacement. Cells show cytoplasmic proliferation with coalescence of fibrils, bizarre forms, and multiple nuclei with basophilic granular stippling designating a degenerative process. Of particular interest in this case are the bone marrow and spleen. The bone marrow also shows definite atypical cellular elements which lie in small clusters and sometimes almost assuming a sheetlike formation. These are reticulum cells which have a weakly staining cytoplasm without granules with occasional vacuoles and a sharply defined nucleous and nuclear membranes which are particularly prominent. Some of these cells contain 2-3 nuclei and mitosis was not seen. Spleen grossly showed a definite increase in weight, normal weight of a spleen in this age group is 30 grams, this spleen however weighed 70 grams.

A lot of this increased weight was probably due to the intensive hyperemia of the organ. Microscopically the spleen does not show as bizarre a picture as that found in the lymph nodes. Giant cells are also abundant here with their oval or kidney shaped nuclei and basophilic granular chromatin. The cells lie singly and in clusters. This cluster formation is seen in the destroyed remnants of the follicles. No mitosis seen and the reticular elements are increased but do not appear to be neoplastic. Then this whole picture when analysed shows that we have a reticulosarcoma of the lymph nodes with a hyperplastic reticular reaction of the bone marrow and spleen.

Discussion

Reticulosarcoma in infants and children is a comparatively rare disease as we can see from the review of the literature. In comparison the disease is much more commonly found in the middle and older age groups. VERHAGEN³⁸⁾ in the available cases up to the time he wrote his paper (1940) showed that in the pediatric group he had only 2 cases and then a very gradual increase till the 40-60 group where he found the greatest incidence. ATTIA⁶⁾ in a study of 124 cases of lymph node biopsy showed that 75% were in the 30-60 age group. Also showed that males were much more frequently involved than females. VERHAGEN³⁸⁾ in his study showed that the incidence was about equal between both sexes. GREIFENSTEIN¹⁶⁾ from his collection of 31 cases showed that all ages affected but over 50% in the 60-70 age group, also that incidence as to sex was men over women 2:1. My analysis of the cases in the pediatric age group showed that the children could be affected from very early infancy, CZERMAK and ROSENKRANZ¹¹⁾ a 3 month old female, through practically every year of the age group. Female children were much more frequently affected than males.

In the cases reviewed we see no one group of glands involved more than another. The process occurred in the upper, lower and peripheral portions of the body. Of interest was the case of AHLSTROEM²⁾ where only the glands of the left popliteal fossa were involved with surgical removal being possible. The case of COMELLI⁹⁾ was of interest because it affected only one organ. The child showed a mass in the loin which could be palpated, child was sent to surgery where a mass was removed from the kidney pole which proved to be a reticulosarcoma of the adrenal with complete destruction of the whole organ. This occurrence where a single organ or group of glands are only involved is certainly more the exception and not the rule. These two cases must be assumed to be early tumors which luckily were diagnosed before invasion and spread could take place.

Clinically these cases of reticulosarcoma had no similarity because of the diversity of the glandular involvement, invasion and spread of the tumor. But if we study the whole group together and see which symptoms occur most frequently then we can set up a criteria divided into three groups:

- A. Diagnosis questionable: These symptoms can occur in a large number of diseases.
1. Anorexia, malaise, easy fatigability.
 2. Persistent cough, light cyanosis and stridor.
 3. Secondary anemia.
 4. Persistent fever fluctuating between 38–39° C. over 3–4 weeks.
 5. Hemorrhagic diathesis and loss of weight.
- B. Diagnosis probable: If leukemia, Hodgkins and infection ruled out.
1. X-ray of lungs reveals a mediastinal enlargement.
 2. Enlargement of one or more of the palpable nodes.
 3. Palpation of nodes or mass in abdomen.
- C. Diagnosis positive:
1. Extirpation or biopsy of a lymph node and histologically investigated.

In children the most frequent involvement of the reticulo-endothelial system is infectious reticulosis and noninfectious reticulosis or as it is sometimes known Letterer-Sives disease. The term reticulosis was first used by EWALD¹³⁾ in 1923 when he tried to include this condition as a third member of the then known lymphatic and myelogenous leukemias. After a number of cases came out in the literature UELINGER³⁷⁾ and DERISCHONOFF¹⁴⁾ came out with a classification of reticulosis. UELINGER³⁷⁾ stated at the same time that reticulo-endothelial reaction was almost always to be found only in children. SIVE³³⁾ who divided reticulosis into an infectious and noninfectious group from a clinical standpoint also stated that this process almost exclusively occurred in children. ABT and DENENHOLZ¹⁾ with their presentation of a case of non-infectious reticulosis choose to call this disease process Letterer-Sives disease. SACKS³¹⁾ described this condition as a malignant reticulo-endotheliosis because there was a proliferation of malignant reticulum cells and histiocytes in the lymph nodes, spleen, bone marrow and liver. He also stated that this disease is found from infancy to senility. STERNBERG³⁴⁾ is also of the opinion that this disease is about equally divided between children and adults. SCHAFER³²⁾ in 1949 combined all the cases in the literature up to that time as nonlipid reticulosis. Number of cases which met his criteria were 24. The main trouble one met in the attempt to classify these reticulosis was that a number of cases did not meet the criteria set up, these cases particularly in the childhood group were those of TCHISTOWITSCH and BYKOWA³⁶⁾, ROUSSY and OBERLING²⁶⁾, BENECKE⁷⁾ from the reviewed literature and KLOSTERMEYERS¹⁸⁾ case of a 13 month old male child with a so-called septic reticulosis but due to the infiltration to the stomach and intestinal tract could be a transition to the reticulosarcoma type. This case was not included in the collection because of its doubtful nature. These cases then show not only a reticulosis but are combined with reticulosarcoma. This question of combinations was taken up by ROSSLE²⁷⁾ due to the mass of literature and diversity of opinions which appeared after

ROULETS²⁷⁾ first paper on reticulosarcoma and his classification of same. This outflow of articles was not only over cases but with other classifications. AHLSTROEM²⁾ divided the reticulosarcomas into (1) undifferentiated, (2) fibrillary differentiated, (3) polymorph cellular form. A much more detailed classification was later proposed by DE OLIVEIRA²⁴⁾ in which he differentiates 6 groups. RÖSSLE²⁵⁾ therefore summarized the whole picture and seems to be of the opinion that reticulosis, reticulosarcoma, reticulo-sarcomatosis and monocytic leukemia are just different gradients of a tumor form of the reticulo-endothelial system. His understanding of reticulosis in particular is always in the sense of being a noninfectious growth, therefore a haemoblastosis. DEELMAN¹³⁾ is of the opinion that reticulosis in a narrow sense is a growth of the reticular cells systematically characterized, benign when it is contained, malignant when the growth is systemic. The question of transition or combination was mentioned rather early by ROULET²⁸⁾ in his second paper where he was of the opinion that reticulosarcoma in its developing stages had something in common with hyperplastic reticulosis. AHLSTROEM³⁾ in a later paper seemed to think that there was some connection between reticulosis and reticulosarcoma and that it was quite possibly for one to go over into the other form. He stated that reticulosis could be an expression of a metastatic deseminatation and that both processes in these cases are of a neoplastic nature. CRACIUN and URSU¹⁰⁾ also bring out this connection with a peculiar picture found in the spleen. This peculiar picture of splenic hyperplastic reticular reaction is often seen in combination with the so-called giant follicular lymphoma (Brill-Symmers disease). The affected nodes in this disease show a increase in the number of giant germinal centers and an increased proliferation of reticulum cells or lymphoblasts. Interesting in this disease is that the spleen in a large number of cases shows a follicular proliferation and a tendency to become the seat of reticulosarcoma as shown by SYMMERS³⁵⁾ and RÜTTNER³⁰⁾. This disease is usually seen in adults. ROULET²⁹⁾ who particularly studied this question of the spleen in reticulosarcoma showed that the spleen contained characteristic lesions similar to those found in the lymph follicles. Isolated groups of cells with multiple nuclei which if the cells form a syncetium will disrupt or destroy the splenic pattern. He agrees with AHLSTROEM³⁾ that this manifestation is probably a histohomologous type of metastasis. The above described picture as found in the spleen was already presented in my histological discription but I believe that the microphotograph shows this even more clearly. There we see 2 arterioles with the remnants of the follicles and there lying enmeshed and within the follicle boundaries are these giant cells with 2-3 nuclei which are indented and kidney shaped, chromatin is of a granular nature. Cells are oval and some appear to have irregular forms. These cells are clustered in the follicles but single cells are seen in the sinuses. No mitotic figures are noticed. This picture in my opinion could be very similar to those cases described by ROULET²⁹⁾ where he believes that this hyperblastic reticulocytic reaction could be called a neoplastic reticulocytic reaction to the so-called histohomologous metastasis called forth by the reticulosarcoma of the lymph nodes. Weither, this reaction called forth

by the sarcoma, is actually a dissemination of malignant cells from the primary tumor or due to some unknown factor proliferated by the malignant cells is as yet an unknown entity and purely hypothetical.

Conclusions

1. Reticulosarcoma can occur in early infancy and in any year of the pediatric age limit, but is a relatively rare disease.
2. Isolated nodular and organ involvement is seen but is extremely rare.
3. Clinically it is practically impossible to set a criteria for diagnosis.
4. Reticulosarcoma is found combined with reticulosis, and that this hyperplastic reaction might possibly be a histohomologous response called forth by the primary reticulosarcoma.

Summary

Case presented of a 8 month old female child in which the condition of reticulo-endothelial involvement only then suspected when a week before death an enlarged inguinal lymph node was seen. Clinical and pathological data presented and discussed. Short discussion of reticulo-endothelial diseases in children plus a discussion of the possibility of a histohomologous reaction giving rise to hyperplastic reticulosis from primary reticulosarcoma of the lymph nodes.

Bibliography

- 1) ABT, H. F., and DENENHOLZ, E. J., Amer. J. Dis. Childhood 51, 499 (1936).
 - 2) AHLSTROEM, C. G., Acta path. scand. 10, 241 (1933).
 - 3) AHLSTROEM, C. G., Beitr. path. Anat. 106, 54 (1941/42).
 - 4) AHLSTROEM, C. G., Virchows Arch. 301, 48 (1938).
 - 5) AHLSTROEM, C. G., Beitr. path. Anat. 108, 169 (1943).
 - 6) ATTIA, O. M., J. royal egypt. med. Ass. 31, 417 (1948).
 - 7) BENECKE, E., Virchows Arch. 286, 693 (1932).
 - 8) CECIL, R. L., Textbook of Medicine, 7th ed. (1948), p. 1114.
 - 9) COMELLI, E., Pediatria 47, 162 (1939).
 - 10) CRACIUN, E. C., and URSU, A., Bull. Ass. franç. 22, No. 9 (1933).
 - 11) CZERMAK, H., and ROSENKRANZ, Öst. Z. Kinderheilk. 51, 167 (1950).
 - 12) DAWSON, E. K., INNES, J. R., and HARVEY, W. F., Edinburgh Med. J. 44, 645 (1937).
 - 13) DEELMAN, H. T., Schweiz. Z. allg. Path. Bact. 12, 137 (1949).
 - 14) DERISCHANOFF, S., Frankf. Z. Path. 41, 184 (1931).
 - 15) EWALD, O., Dtsch. Arch. klin. Med. 142, 222 (1923).
 - 16) GREIFENSTEIN, A., Arch. Ohren- usw. Heilk. 143, 189 (1937).
 - 17) GROSSO, E., Minerva Ped. 1, 236 (1949).
 - 18) KLOSTERMEYER, W., Beitr. path. Anat. 93, 1 (1934).
 - 19) KNOPF, E., Arch. Kinderheilk. 134, 129 (1947).
 - 20) LANG, H. B., and ZIERHUT, H., Öst. Z. Kinderheilk. 4, 225 (1950).
 - 21) LETTERER, E., Frankf. Z. Path. 30, 377 (1924).
 - 22) MITCHELL, A. G., and NELSON, W. E., 4th ed. (1948), p. 27.
 - 23) NOBICOURT, P., and LIEGÉ, R., Bull. Soc. Péd. Paris 34, 91 (1936).
 - 24) OLIVEIRA, DE G., Virchows Arch. 298, 464 (1936).
 - 25) RÖSSLE, R., Beitr. path. Anat. 103, 385 (1939).
 - 26) ROUSSY, G. E., and OBERLING, CH., Wien med. Wschr. 1934, 15.
 - 27) ROULET, F., Virchows Arch. 277, 15 (1930).
 - 28) ROULET, F., Virchows Arch. 286, 702 (1932).
 - 29) ROULET, F., Schweiz. Z. allg. Path. Bact. 10, 88 (1947).
 - 30) RÜTTNER, J. R., Schweiz. Z. allg. Path. Bact. 13, 92 (1950).
 - 31) SACKS, M. S., Arch. Path. 26, 676 (1938).
 - 32) SCHAFER, E. L., Arch. Path. 48, 462 (1949).
 - 33) SIVE, S. A., Z. Kinderheilk. 55, 212 (1933).
 - 34) STERNBERG, C., Ergebn. Path. 30, 1 (1936).
 - 35) SYMMERS, D., Arch. Path. 34, 385 (1942).
 - 36) TSCHISTOWITSCH, F., and BYKOWA, Virchows Arch. 267, 91 (1928).
 - 37) UELINGER, G., Beitr. path. Anat. 83, 197 (1931).
 - 38) VERHAGEN, H., Z. Krebsforsch. 50, 163 (1940).
 - 39) VIDEBAEK, A., Acta Paediatrica 37, 502 (1950).
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